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BURNS DOANE SWECKER & MATHIS L L P
POST OFFICE BOX 1404
ALEXANDRIA VA 22313-1404

EXAMINER	
BRUSCA, J	
ART UNIT	**PAPER NUMBER**
1631	29

DATE MAILED: [illegible]

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

PTO-90C (Rev. 2/95)
*U.S. GPO: 2000-473-000/44602

1- File Copy

Office Action Summary	**Application No.** 09/132,231	**Applicant(s)** HORWITZ ET AL.	
	Examiner John S. Brusca	**Art Unit** 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☑ Responsive to communication(s) filed on *14 April 2000 and 28 April 2000* .

2a)☑ This action is **FINAL**. 2b)☐ This action is non-final

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☑ Claim(s) *3,4,6-8 and 11-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☑ Claim(s) *7,8,11,12,19,20 and 27* is/are allowed.

6)☑ Claim(s) *3,4,6,13-18 and 21-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____
18) ☐ Interview Summary (PTO-413) Paper No(s) ___
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. The suspension of the instant application stated in the Office action mailed 7/5/00 is lifted and prosecution of the instant application is resumed. This Office action contains all remaining grounds of rejection.

Specification

2. The instant application is now in compliance with the sequence rules in view of the amendment received 4/28/00.

Claim Rejections - 35 USC 112

3. The rejection of claims 3, 4, 6, 7, and 12-25 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendment received 4/14/00.

Claim Rejections - 35 USC 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

5. Claims 3, 4, 6, 13-18, and 21-25 and newly filed 26 are rejected under 35 U.S.C. 102(e) as being anticipated by Pieczenik

6 The claims are drawn to methods of making, screening, and isolating populations of vectors that express a polypeptide with a biological activity, wherein the molecule is expressed from sequences isolated from a population of random sequences synthesized by enzymatic or chemical methods. In some embodiments the method isolates host cells comprising the selected vector, the polypeptide reacts with a substrate, the polypeptide is isolated, and the population of random sequences comprises about a billion members.

7. Pieczenik claims in claims 1-92 methods of making, screening, and isolating populations of vectors that express a polypeptide epitope, and the isolated polypeptides, wherein the epitope is expressed from sequences isolated from a population of random sequences. Claim 13 specifically teaches synthesis of the random sequence nucleic acid by chemical methods. Host cells comprising the random sequences are taught in claims 1, 23, 24, 34, and 90. In claims 47, 77, and 90 Pieczenik shows epitopes encoded by random sequences of nucleic acid that bind to an antibody, which is equivalent to the claimed polypeptides that react with a substrate. Pieczenik shows populations of vectors comprising random nucleic acid sequences or polypeptides with at least 10% of all possible random sequences in claims 10, 24, 34, 36, and 47, which is equivalent to up to 4x10^{15} peptides and up to 4x10^{21} nucleic acids.

8 Applicant's arguments filed 4/14/00 and 4/28/00 have been fully considered but they are not persuasive.

9 The Declaration filed on 9/24/99 under 37 CFR 1.131 has been considered but is ineffective to overcome the Pieczenik reference because it is not executed. Until such time as the applicants provide an executed declaration under 37 CFR 1.131 the rejection under 35 U.S.C. 102(e) over Pieczenik will be maintained. **An executed declaration will be sufficient to**

overcome the rejection over Pieczenik. In addition the declaration did not include copies of the laboratory notebook referred to in the declaration, and should be included with any further submission of an executed declaration if such declaration refers to notebook pages.

10 Although the Pieczenik reference is a U.S. patent, upon further review the claims of the Pieczenik reference do not claim the same invention as the instant application, and therefore a declaration under 35 U.S.C. § 131 is sufficient to overcome the above rejection. The differences between the claimed invention of Pieczenik and the instant application are as follows: a) Pieczenik claims nucleic acids and their methods of making that encode epitopes that represents a non-obvious species of the instant claimed nucleic acids and their method of making that encode a desired biological property; b) Pieczenik does not disclose or claim biased random nucleotides that have a reduced level of stop codons; c) Pieczenik does not disclose or claim random sequences that are enzyme substrates; d) Pieczenik does not disclose or claim methods of making random sequence polynucleotides by use of terminal transferase.

11. Regarding the Declarations under 37 CFR 1.608(b) by Phillip A. Patten received on 4/28/00 and 6/1/00, the Declaration asserts that the Pieczenik patent disclosure does not enable (in the claimed parent applications 07/301258 and 06/770390) the claimed invention of screening for epitopic peptides. The parent applications of Pieczenik disclose use of a lambda phage vector to express random peptide sequences. Inherent in the use of a lambda phage vector is the lysis of the host cell. Therefore the random peptide expressed by a lambda phage clone (usually in the form of an individual plaque from a single phage clone) also comprises a wide range of host cell proteins. The Patten Declaration asserts that such a wide array of host cell proteins would prevent one of skill in the art at the time of filing of the Pieczenik parent applications from

detecting the presence of an expressed random peptide because of the wide range of epitopes present in the host cell. The Declaration asserts that antisera would react with host cell proteins and therefore prevent detection of reaction of antisera that is specific for an epitopic peptide expressed by a lambda phage clone.

12. The Examiner provides a copy of DeWet et al. which shows that prior to the time of filing of the earliest Pieczenik parent application it was known in the art to use antisera that was preadsorbed with host cell proteins to prevent detection of reaction between a test antisera and host cell proteins. See page 438, second column through page 439, second column, and the entire publication for successful results of their method.

13. It is the Examiner's opinion that the earliest Pieczenik application is enabled for detection of expressed epitopic peptides by use of lambda phage vectors. Although some possible epitopes might be absorbed by the method of DeWet et al., and some possible epitopes might not react with available antisera, such as naive antisera, one of skill in the art would be able to test and screen an expression library expressing random epitopes and produce a wide range of positive results that span the full range of possible epitopes in the library.

14. The Applicants state that the Kauffmann applications claim interfering subject matter. However it is the Examiner's position that the Kauffmann applications do not disclose fully random peptide sequences, because the term stochastic used and claimed by Kauffmann was never defined in the Kauffmann applications as meaning random, and the examples of stochastic sequences disclosed in the Kauffmann applications do not result in fully random sequences. Rather, the examples in the Kauffmann U.S. Patent No. 5,723,3232 result in sequences that are not fully random (see attached notes outlining the exemplified methods of Kauffmann).

Therefore the Examiner believes that the Kauffmann applications do not claim interfering subject matter

Double Patenting

15 The terminal disclaimer filed on 4/14/00 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. Patent No. 5,824,469 has been reviewed and is accepted. The terminal disclaimer has been recorded

16. The rejection of claims 3, 4, 6, 13, and 15-25 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2 and 3 of U.S. Patent No. 5,824,469 is withdrawn in view of the terminal disclaimer received 4/14/00.

Conclusion

17. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca, Ph.D. whose telephone number is (703) 308-4231. The examiner can normally be reached on Monday-Friday 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward can be reached on (703) 308-4028. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-7939 for regular communications and (703) 305-7939 for After Final communications.

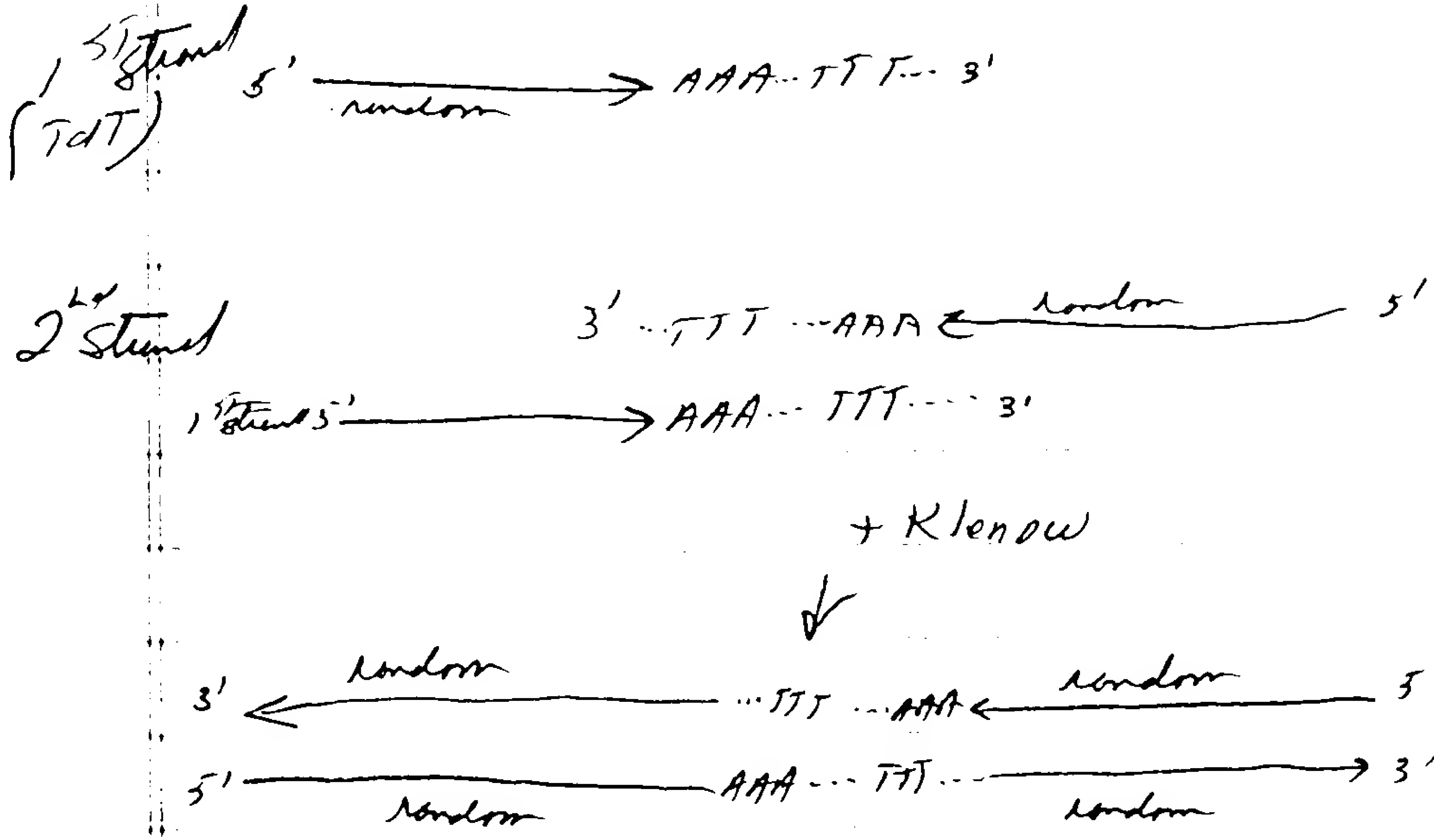
Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

John S. Brusca, Ph.D.
Primary Examiner
Art Unit 1631

jsb
February 23, 2001

1st method

Kaufmann 5,723,323

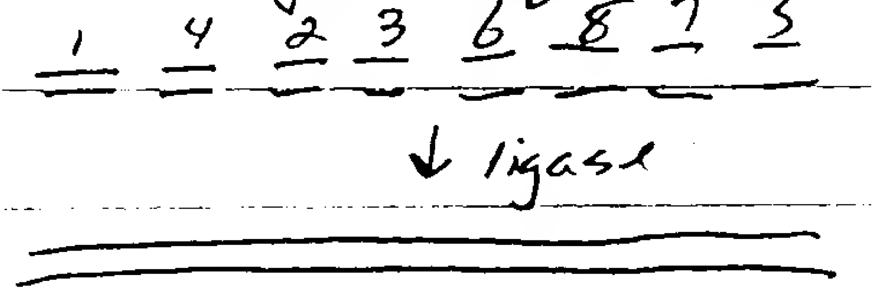


→ not totally random sequence.

Random has deficit of T to avoid stop codons.

2nd method

ligate short (8mer) oligos without stop codons. (example uses only 5 oligos, each is a palindrome & forms ds DNA, ligate them to form random oligomers of ds palindromes)



→ not totally random sequence.

insert to vector

also Column 8 L 35-43 vague

For Proteins, Col. 14, say get them from the DNA clones.
or alternatively bizarre biochemical peptide synthesis scheme. Col. 15-16